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Diffusion Weighted MR Imaging in Acute Stroke: the SGH Experience

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ABSTRACT

Cerebrovascular accident (CVA) is a leading cause of death and disability in many countries. Diffusion-weighted (DW) magnetic resonance (MR) imaging has been reported to be useful in the detection of acute strokes and as an investigative tool evaluating the therapeutic effects of neuroprotective and thrombolytic agents. The objectives of this study are to share our experience using the commercially available isotropic DW scan in imaging of acute stroke, assess its usefulness over conventional T2-weighted (T2W) scans in a busy clinical radiology unit and highlight it pitfalls. We found the rapid sub-minute DW technique well suited for ill and restless stroke patients and superior to T2W scans in many ways. It was highly sensitive to acute ischaemic lesions, made lesions easily identifiable and readily differentiated the acute lesion from a background of multiple chronic infarcts. However, there are potential pitfalls in the evaluation of small hyperacute posterior fossa strokes and venous infarcts. The major strength of this MR technique lies in its ability to diagnose hyperacute strokes and thence the potential for therapeutic thrombolysis, but unfortunately patients qualifying for the "therapeutic window" were a minority. More efforts need to be focused on public education in order for this powerful imaging modality to find its true value and contribute to viability of an effective thrombolytic programme.

Keywords: acute stroke, diffusion-weighted MR, T2-weighted MR, strengths, pitfalls

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INTRODUCTION

Cerebrovascular accident (CVA) remains the leading cause of death and disability in many countries and the third leading cause of mortality in Singapore[1]. The sensitivity of diffusion-weighted (DW) magnetic resonance (MR) imaging to ischaemic brain injury within minutes after the onset of the ictus[2-6] has revolutionised the way we evaluate stroke. This imaging technique has furthered our understanding of stroke pathophysiology, and plays a potentially crucial role in guiding us in the therapeutics of acute stroke[3,5]. Active research is ongoing in investigating efficient neuroprotective and thrombolytic therapies in acute stroke. Early detection and diagnosis are keys to this therapeutic strategy.

The objectives of our study are to describe our experience with the commercially available isotropic DW scan in acute stroke imaging, assess its usefulness over conventional T2-weighted (T2W) MR imaging in a busy radiology service, and highlight its potential pitfalls.

MATERIALS AND METHODS

Twenty-two consecutive patients (13 men, nine women; aged 25-79 years, mean 57.2 years) clinically diagnosed to have acute stroke and who had hyperintense lesions correlating with their acute neurological deficits on DW scans performed within 48 hours were included in our study. The onset of the ictus was taken as the time when patient was last known to be well. There were four (18.2%) patients imaged within the first six hours inclusive, three (13.6%) between six to 12 hours inclusive, six (27.3%) between 12 to 24 hours inclusive, and nine (40.9%) between 24 to 48 hours inclusive (Table I). Eight (36.4%) patients had follow-up CT and/or MR scans. Six (27.3%) patients had lacunar infarcts from small vessel disease, fifteen (68.2%) from large vessel disease, and one (4.5%) had venous infarcts from cerebral venous thrombosis (Table I).

The studies were performed on a 1.5 Tesla MR system with echo-planar (EP) capability (Vision system, Siemens Medical Systems, Erlangen, Germany). A circularly polarised head coil was used for transmitting and receiving. Each patient had a turbo spin-echo T2W scan (TR 5400 ms, TE 99 ms, 286 x 512 matrix), and an isotropic multislice, single-shot spin-echo echo-planar DW sequence using a diffusion sensitivity of b = 1000 s/mm^2 (TR 123 ms, TE 80 ms, 128 x 128 matrix). The isotropic DW sequence was

employed to minimise the effects of diffusion anisotropy[7,8]. Typical scan parameters for both sequences were: 230 mm field of view, twenty 5 mm axial sections with 1 mm interslice gap. Other standard MR sequences, MR angiography, as well as investigations including echocardiogram, carotid ultrasound, and laboratory tests such as markers for collagen vascular disease were also obtained, but beyond the scope of this paper.

The DW and T2W scans were randomised and separately reviewed by two neuroradiologists, and final consensus was reached in cases of dispute. The readers were informed of the clinical neurological deficits, but blinded to the timing of the ictus. The scans were evaluated for the number of lesions that correlated with the clinical findings, their size and conspicuity grading. T2W-hyperintense lesions that did not correlate with acute neurological deficits, or had clinical or imaging evidence of chronicity were excluded. Discrete and distinct lesions were counted as separate. The lesions were arbitrarily subdivided into small (maximum diameter less than or equal to 15mm) or large (greater than 15 mm) lesions based on size. Lesion conspicuity was graded: 0 = not seen, 1 = doubtful hyperintensity, 2 = definite but subtle hyperintensity, 3 = obvious hyperintensity, and 4 = glaringly obvious hyperintensity (could not be missed). We evaluated the tabulated results for how the conspicuity of the lesions on DW imaging was affected by their size, location or timing of the ictus to imaging.

Table I. Summary of patients and lesions according to time of MR from ictus.

Timing of scan (h)	0 - 6	6 - 12	12 - 24	24 - 48	Total
No. of patients	4	3	6	9	22
Cause of acute stroke					
small vessel disease	1	0	0	5	6
large vessel disease	3	3*	5	4	15
venous infarcts	0	0	1	0	1
Multiplicity of lesions					
single lesion	4	1	3	7	15
multiple lesions	0	2	3	2	7

* watershed infarct.

Table II. Evaluation of Lesion Conspicuity on DWI and T2W.

Timing of scan (h)	0 - 6	6 - 12	12 - 24	24 - 48	Total
No. of lesions	4	7	14	13	38
Size of lesions					
small	2	6	6	10	24
large	2	1	8	3	14
Conspicuity score					
On DWI					
grade 0	0	0	0	0	0
grade 1	0	0	0	1	1
grade 2	1	0	1	1	3
grade 3	1	0	2	0	3
grade 4	2	7	11	11	31
On T2W					
grade 0	4	0	0	0	4
grade 1	0	1	0	0	1
grade 2	0	2	4	2	8
grade 3	0	3	8	4	15
grade 4	0	1	2	7	10
(A) DWI > T2W	4	6	9	4	23
(B) T2W > DWI	0	0	1	2	3
(C) DWI = T2W	0	1	4	7	12
T2W < 3	4	3	4	2	13
DWI < 3	1	0	1	2	4

RESULTS

The results were tabulated in Tables I and II. A total of 38 lesions in 22 patients satisfied the inclusion criteria. Fifteen (68.2%) patients had single lesions, and seven (31.8%) had multiple lesions (Table I). Twenty-four of the 38 lesions (63.2%) were small, and 14 (36.8%) were large (Table II).

The conspicuity grading of lesions on T2W and DW scans was summarised in Table II. By comparing lesional conspicuity on the two scans, the lesions were categorised into three groups: (A) lesions more conspicuous on DW scans, 23 (60.5%); (B) lesions more conspicuous on T2W scans, three (7.9%); and (C) lesions equally conspicuous on both, 12 (31.6%). Of the 23 lesions more conspicuous on DW scan, four were invisible on T2W (conspicuity score of zero) (Figs. 1 and 2). All four lesions were hyperacute infarcts imaged within six hours from the ictus (small, n = 2; large, n = 2). The three lesions better seen on T2W scan scored 1-2 on DW scan (small, n = 3). Two of these were in the brainstem (medulla and pons) and imaged 24-48 hours from ictus (Fig. 3), and the third was a high frontal convexity venous infarct imaged 12-24 hours from ictus. There were no acute T2-hyperintense lesions which scored zero on DW scan.

There were 31 (81.6%) glaringly obvious lesions (conspicuity grading 4) on DW scans (small, n = 19; large, n = 12) (Table II). Of the 19 small lesions (Fig. 4), five (26.3%) were similarly graded on T2 imaging but there were six (31.6%) lesions that were only subtle or doubtful hyperintensities on T2W scans. Except for the first six hours, more than 75% lesions in each time frame were graded 4 on DW scans. In contrast only 10 (25%) lesions scored 4 on T2W scans (small, n = 5; large, n = 5). Only lesions imaged at 24-48 hours had a majority (seven of 13 lesions, 54.5%) that were highly conspicuous on T2W scans.

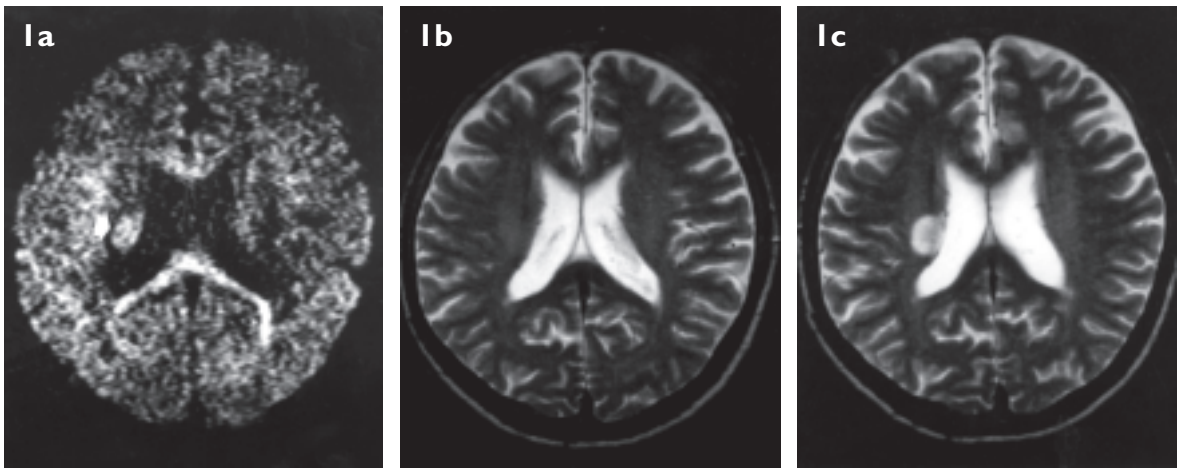

Fig. 1 (a) DW scan at five hours post-ictus demonstrates definite small hyperintensity (arrow) in the right corona radiata (scored 3), corresponding to patient's acute left sided weakness. (b) T2-weighted scan at the same level shows no discernible infarct, even in retrospect. (c) T2-weighted scan on day 6 reveals interval appearance of lacunar infarct.

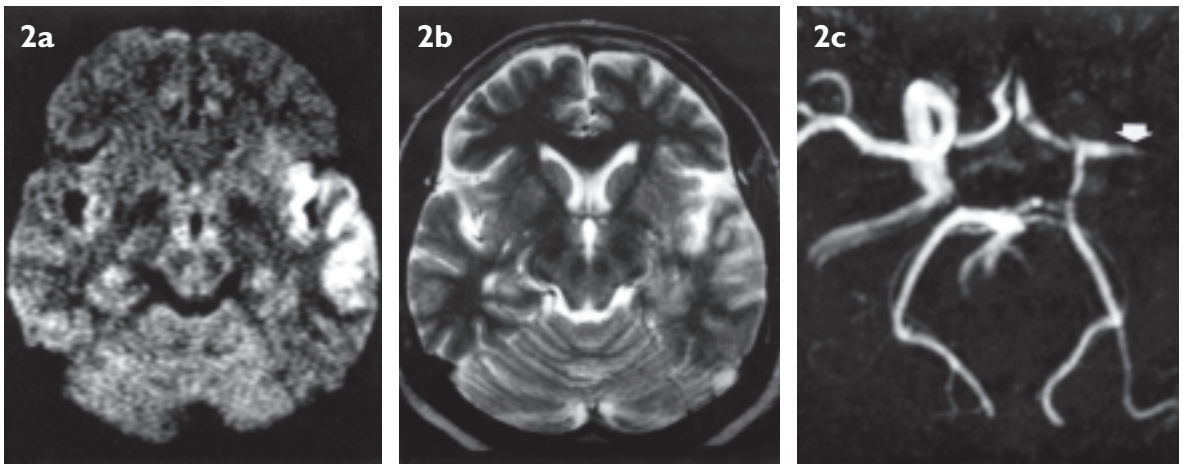

Fig. 2 (a) DW imaging at 4.5 hours post-ictus shows indisputable large cortical infarct in the left middle cerebral artery territory, graded glaringly obvious on conspicuity scoring. (b) This is deemed obscure on T2-weighted scan. (c) MR angiography reveals abrupt cut-off of the M1 segment of the left middle cerebral artery (arrow).

Seven lesions scored less than four on DW scans (Table II). These were: two small brainstem lesions imaged 24-48 hours, three venous infarcts in a patient with superior sagittal sinus thrombosis imaged at 12-24 hours, and two lesions imaged less than six hours from ictus. The two large hyperacute lesions had conspicuity scores of 2 and 3 (including a patient imaged at 30 minutes post ictus).

DISCUSSION

DW imaging detects random movement of water protons by incorporating balanced gradient pulses into a standard spin echo sequence[2,9]. Static water protons get dephased and rephased with zero net translation. In contrast, randomly diffusing water protons lose phase coherence, resulting in net translational movement. In DW images static water protons are hyperintense (bright signal); and the greater the net translation, the greater the signal loss. Since the water protons in normal brain parenchyma and cerebrospinal fluid contain random Brownian motion, these appear dark on DW images. The more rapid free diffusion of water protons in CSF results in a darker signal relative to normal brain tissue. In ischaemic injury, the random movement of water protons is rapidly restricted due to the presence of cytotoxic edema. This results from failure of the sodium-potassium ATPase pump at the cell membrane, leading to an influx of extracellular water protons and ions into the intracellular space. Hence, ischaemic tissue shows up as a hyperintense area on DW images, reflecting an area of impaired diffusion.

In addition to the diffusibility of water protons, the signal intensity of a DW image is also dependent on presence of tissue diffusion anisotropy (differential water diffusibility due to tissue orientation), such as in white matter tracts. Traditionally, the DW sequence comprises of three sets of anisotropic DWI images, where the diffusion gradient pulses were separately applied in three orthogonal axes. The radiologist evaluates each set of images for areas of hyperintensity keeping in mind the direction of the diffusion gradient

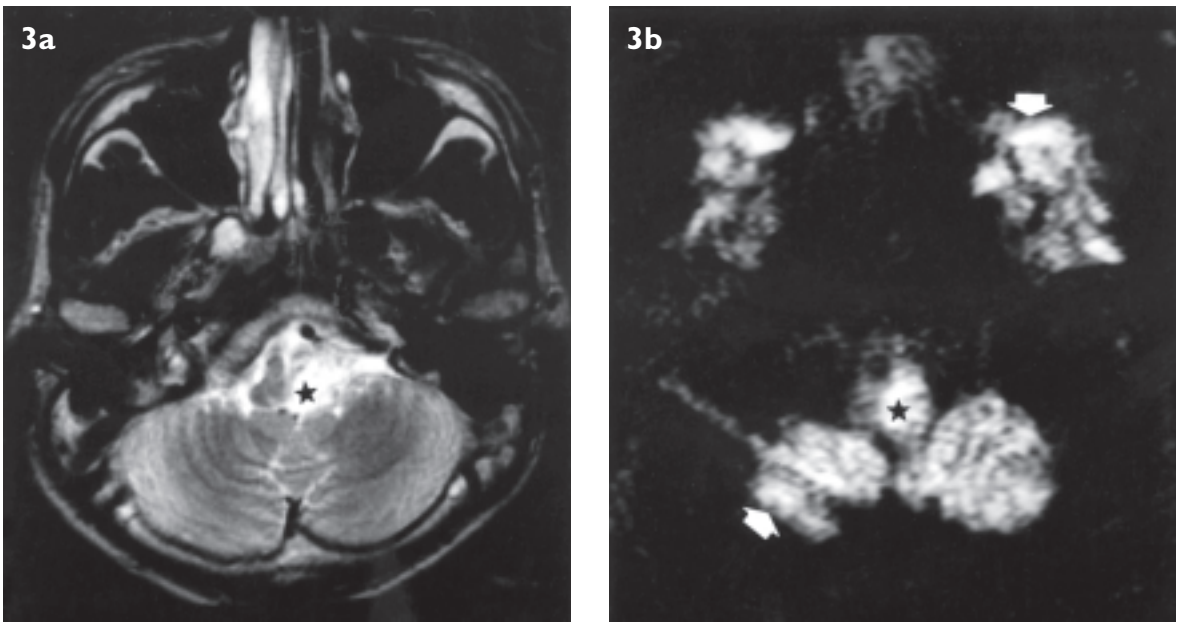

Fig. 3 (a) T2W scan at the level of the medulla shows an acute left medullary infarct (black star) graded 3 on conspicuity score, at 24-48 hours post-ictus. (b) Left medullary hyperintensity (black star) is made less obvious (scored 2) on DW imaging by distracting susceptibility artefacts (white arrows).

pulse, and the confounding effects of tissue orientation. The commercially available isotropic DW scan reduces the effects of anisotropy by taking the average diffusion in three orthogonal planes[7,8]. Studies had shown that isotropic DW imaging was just as effective as orthogonal axis DW imaging in the clinical evaluation of acute stroke[7]. The single isotropic DW image set generated was less cumbersome to review and allowed for quick interpretation. In addition, it was more practical on our picture archiving and computer system (PACS) in our high volume clinical service. However, we noted two anisotropy artefacts consistently identified on all our isotropic DW images. These were in the splenium of the corpus callosum and the superior cerebellar decussation in the brainstem.

Our results showed clear advantages of the isotropic DW scan over the T2W scan in evaluation of acute stroke. Lesion visibility was highly accentuated on DW imaging, with more than 75% lesions imaged at 6-48 hours graded glaringly conspicuous, and 60% of all lesions graded more conspicuous on DW than T2W scans. The suppression of diffusion signal from normal background brain tissue and cerebrospinal fluid increases the lesion contrast[5]. This principle is similar to how magnetisation transfer suppression improved the contrast and detection of enhancing lesions[10]. In addition, background "T2-shine through" effects further contribute to lesion visibility on DW images[7]. This is because diffusion gradient pulses are usually incorporated on a T2-weighted image. Hence, hyperintense signal on DW images may be contributed by actual impaired diffusion in the tissue, or inherent T2 relaxation characteristics of the tissue imaged. This "light bulb" effect made interpretation of DW scans fairly effortless[11].

Generally, the size of an infarct did not limit its conspicuity on DW scans. Indeed five of six small T2W subtle or doubtful lesions (graded 1 or 2) were glaringly conspicuous on DW scans (Table II). We attributed this again to the excellent lesion contrast[11]. This quality of DW scans clearly aided detection of small infarcts that might otherwise be less obvious to the untrained eye on conventional MR scans.

We also found the DW scan distinctly useful in readily singling out the acute infarct from a multitude of chronic subcortical lacunes in one patient imaged at 24-48 hours (Fig. 4). This was difficult on the T2W scan alone, even with the benefit of clinical input. In addition, identification of separate acute lesions in different vascular territories on the DW scan readily suggested an underlying embolic or thromboembolic pathophysiology[4,7].

Our results concurred with the literature[2,4-6] attesting to the superiority of DW imaging over conventional T2W scans in its unique sensitivity to hyperacute strokes. All 4 hyperacute infarcts in our cohort were evident on DW imaging but occult on T2W scans (Figs. 1 and 2). One such patient was imaged at 30 minutes after she became symptomatic on the angiography table. The subtle DW hyperintensity in the middle cerebral artery territory was graded 2. The earliest ischaemic injury detected on DW imaging in a human subject had been previously reported at 39 minutes post-ictus[6].

Unfortunately, only two of our acute stroke patients (8.7%) were imaged within the putative optimal

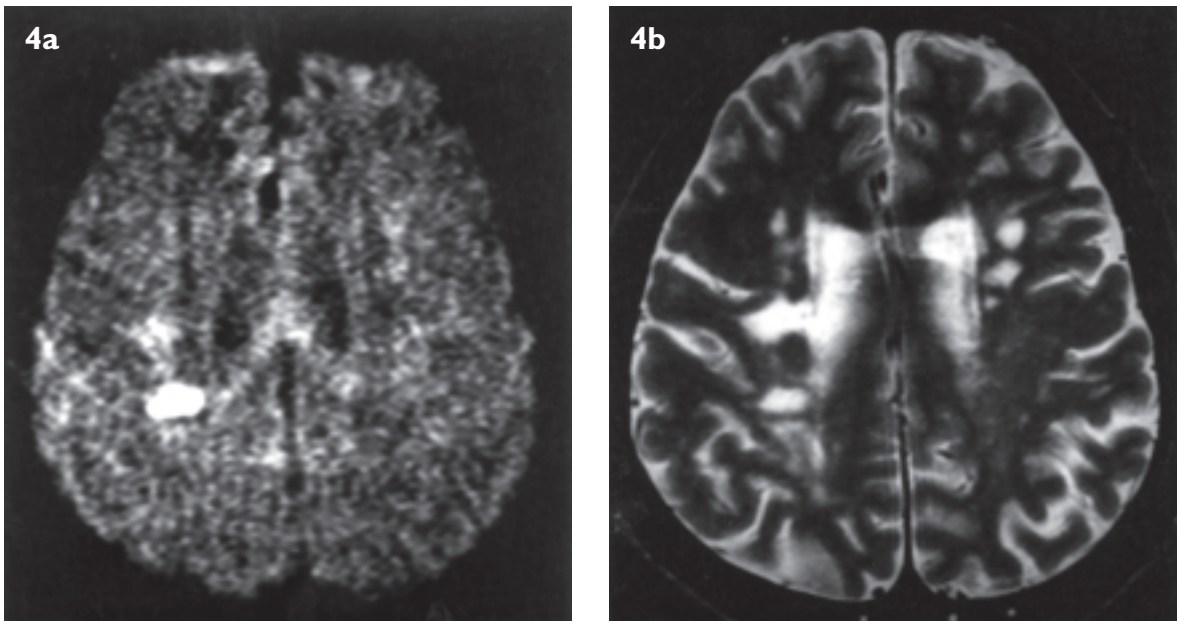

Fig. 4 (a) DW scan at 24-48 hours post-ictus unambiguously identifies the acute infarct (graded 4) in the posterior right corona radiata. (b) T2-weighted scan demonstrates multiple subcortical lacunar infarcts (scored 3), but distinguishing the acute lesion is impossible even with clinical input.

three-hour "therapeutic window". In order to fully utilise the unique sensitivity of DW imaging for hyperacute infarcts[2,4-6] and contribute to viability of an effective thrombolytic programme, more needs to be done to increase stroke awareness of the public and hospital staff so as to improve patient triage in the emergency room and change the tardy mindset of some towards emergent stroke care[5,11].

Our results highlighted some potential pitfalls of DW imaging. Small lesion size did not affect lesional conspicuity generally, but all three lesions were more obvious on T2W than DW scans were small. We believed the location of these two brainstem and frontal convexity infarcts next to image distortion and magnetic susceptibility artefacts was the dominant cause for inferior DW lesion visibility (Fig. 3), by interfering with lesion detection[12]. These artefacts are inherent in echo planar techniques and rife at abrupt interfaces between air and tissue (e.g. the skull base and paranasal sinuses). Lovblad et al found the half-Fourier single-shot turbo spin-echo (HASTE) DW imaging technique superior to the echo-planar DW technique in the posterior fossa due to freedom from image distortions and susceptibility artefacts[9].

Whilst there was clear DW superiority over T2W scans in lesional conspicuity and sensitivity to hyperacute strokes, our earliest hyperacute infarcts were not invariably graded 4 (glaringly conspicuous) on DW imaging. Two of our large hyperacute infarcts (n = 4) only scored 2-3 (Table IV). This relatively reduced conspicuity of the earliest hyperacute infarcts even on DW scans, especially when they are small and located in artefact-fraught areas, serves as a potential pitfall in their detection.

Venous and arterial infarcts are not always clinically distinguishable in the acute phase. However, they have differing features on DW imaging which might reflect different underlying pathophysiology[13,14]. Our patient with venous infarcts was such a case in point. It had been postulated that disruption of the blood brain barrier occurred early in venous infarcts[13,14]. This resulted in early and prominent vasogenic oedema, with mild cytotoxic oedema. Whilst vasogenic and cytotoxic oedema were the equally hyperintense on T2W imaging, vasogenic oedema in venous infarcts contained increased diffusion and was therefore hypointense on DW imaging compared to the hyperintense cytotoxic oedema in arterial ischaemia. In addition, haemorrhagic changes frequently associated with venous infarcts, but absent in our case, might further reduce visibility of venous infarcts on DW scans due to susceptibility artefacts from the blood products.

CONCLUSION

In conclusion, we found the sub-minute ultra-fast isotropic DW scan ideal for frequently ill and restless acute stroke patients. It offered excellent sensitivity to acute stroke lesions and high ease to interpretation due to high lesional conspicuity, readily differentiated acute from chronic infarcts, and in some cases shed light upon the underlying pathophysiology. However, one should also be cognisant of its potential pitfalls, especially in small hyperacute lesions in the posterior fossa and venous infarcts.

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